PHYSIOLOGICAL ANALYSIS OF THE COURSE OF STAPHYLOCOCCAL TOXEMIA IN DOGS IN DIFFERENT AGE PERIODS

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Investigations in this laboratory [1, 2, 5-10] have shown that the action of various bacterial toxins on dogs and puppies over 2-2½ months old is characterized by a standard sequence of changes in the cardiac rhythm, consisting of four phases. Bradycardia first develops, followed by tachycardia, and if lethal doses are given, this gives way to collapse, which itself consists of two phases: 1st – syncope and vagus escape, and 2nd – a change to automatic rhythm or fibrillation. The duration of the phases varies depending on the specific properties of the toxin.

The adaptive importance of the initial bradycardic phase, described by I. A. Arshavskii [3, 4] as anabolic, was established for its severity determines the duration of maintenance of homeostasis in the tachycardiac phase and also the time of onset of collapse and death of the animal. The object of the present investigation was to study in greater detail the course of staphylococcal toxemia, especially during the first two phases. In particular, we investigated the changes in basal metabolism taking place during the first, bradycardic phase.

EXPERIMENTAL METHODS

Experiments were performed on dogs in three age groups: puppies aged between 5 and 14 days days (group 1), puppies aged between 18 and 40 days (group 2), and adult dogs and puppies over 2-2½ months old (group 3). Staphylococcal toxin (Institute of Experimental Medicine, AMN SSSR, batch 196) was injected in doses of between 0.2 and 1 ml/kg intravenously. Recordings were made of the ECG, respiration, and the EEG ona four-channel electroencephalograph. For recording the EEG needle electrodes were used (bipolar leads); these were implanted in the cranial bones at the site of projection of the sensorimotor area of the cortex. Respiration was recorded by means of an electrolytic detector. Changes in body temperature also were recorded. In a special series of experiments the oxygen consumption was measured by Grad's method.

EXPERIMENTAL RESULTS

The absolute lethal dose of staphylococcal toxin when injected intravenously into the animals of all age groups was 0.5 ml/kg. However, the adult dogs and puppies over 2-2½ months old in most cases died within 16-18 h after receiving these doses, and the younger puppies within 1½-3 h. The maximal dose tolerated by the animals of all age groups was 0.2 ml/kg.

In the dogs and puppies of group 3, after injection of staphylococcal toxin in lethal doses (0.5-1 ml/kg), changes in the cardiac rhythm took place in four phases, similar to those developing after administration of dysentery, diphtheria, and typhoid toxins.

After intravenous injection of staphylococcal toxin in a dose of 0.5 ml/kg, the initial bradycardic phase lasted for 1 h 25 min-2 h, and was followed by a tachycardic phase lasting 16-18 h. Between 7 and 8 min before death the dogs developed a transient collapse, showing the two phases described above. An increase in the dose of staphylococcal toxin to 0.75 ml/kg shortened the bradycardic phase to 50-55 min and the tachycardiac to 3½-6 h. After injection of staphylococcal toxin in a dose of 1 ml/kg, the duration of the bradycardic phase was shortened to 20-25 min, and the duration of the tachycardiac phase to 1 h 25 min-24 h 45 min. Hence, the larger the dose of staphylococcal toxin, the less pronounced the bradycardic phase, the shorter the tachycardia, and the sooner the animals died if the doses were lethal.

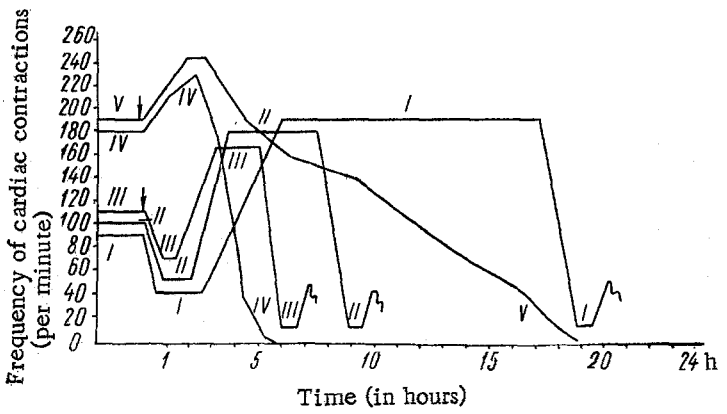

Fig. 1. Schemes of the phases of the changes in the heart rate in adult dogs (I, II, III) and in young puppies (IV, V) after intravenous injection of staphylococcal toxin in doses of 0.5 ml/kg (I), 0.75 ml/kg (II), 1 ml/kg (III), 0.5 ml/kg (IV), and 0.5 ml/kg (V).

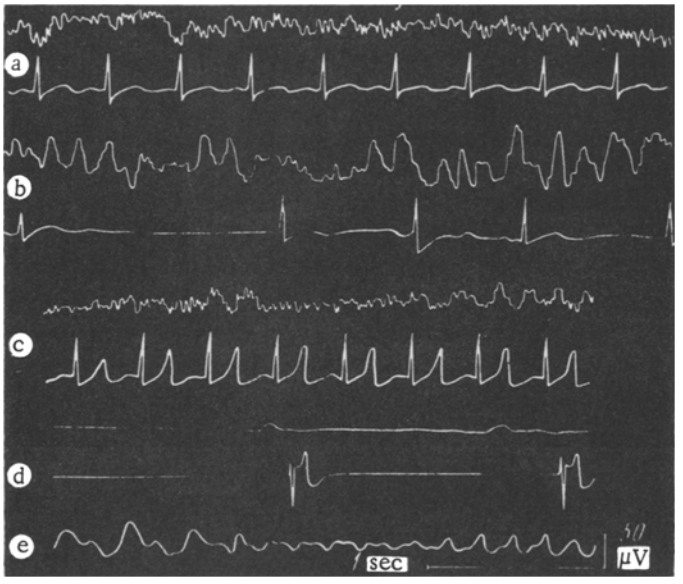

Fig. 2. Changes in the EEG and ECG of adult dogs after intravenous injection of staphylococcal toxin in a dose of 0.75 ml/kg. A) Initial background; B) bradycardic phase 20 min after injecting; C) tachycardiac phase 1 h later; D,E) stages of collapse: atrioventricular rhythm (D) and fibrillation (E).

The relationship between the duration of the tachycardiac phase and the rate of onset of collapse, on the one hand, and the severity of the initial bradycardia on the other, is given in Fig. 1. This shows that the duration of the successive phases during the action of the same toxin depends on the dose.

The bradycardic phase of staphylococcal toxemia was characterized, not only by a slowing of the heart rate, but also by slowing the respiration and synchronization of the electrical activity of the brain, a small drop in the body temperature, and a fall of arterial pressure. The results of an experiment on an adult dog after injection of staphylococcal toxin in a dose of 0.75 ml/kg are given in Fig. 2. In the bradycardic phase the cardiac rhythm was

Oxygen Consumption in the Bradycardic Phase of Staphylococcal Toxemia in Puppies Aged 2-2½ months

Expt. No.	Age	Oxygen consumption (in ml/kg/min)		Decrease (in %)
		initially	in bradycardic phase	
1	2½ months . . .	10,1	8,4	—16,8
2	2½ » . . .	9,0	6,3	—30,0
3	2½ » . . .	12,6	8,9	—28,4
4	2½ » . . .	15,5	12,5	—19,3
5	2½ » . . .	12,9	9,7	—24,8
6	2½ » . . .	15,1	12,6	—16,6
7	2½ » . . .	14,1	8,1	—42,6
8	2½ » . . .	11,6	5,6	—51,7
9	Adult dog	4,1	3,4	—19,1

slowed, respiration was arrhythmic, and the electrical activity on the EEG was synchronized, consisting predominantly of high-amplitude waves with a rhythm of 4-6/sec. Flattening of the P and T waves could be seen on the ECG. Often in this phase an inverted T wave was present. One hour after injection of the toxin the change to the tachycardiac phase took place. The heart rate rose to 220/min, the respiratory arrhythmia disappeared, and the amplitude of the P and T waves increased. In some experiments in this phase a very marked increase in the amplitude of the T waves was observed. The EEG showed an increase in the frequency of the potentials and a lowering of their amplitude. After 4 h the tachycardiac phase changed to the phase of collapse, with the appearance of an atrioventricular rhythm without a P wave and with disappearance of the electrical activity of the cortex, subsequently changing to fibrillation.

Administration of atropine to the experimental animals suppressed the appearance of the initial bradycardia during staphylococcal toxemia, as was also observed after administration of dysentery and typhoid toxins [4, 9].

If the bradycardic phase, the mechanism of which is cholinergic, is in fact anabolic, this must be reflected in metabolic changes. To verify this hypothesis, a series of experiments was carried out to investigate the changes in oxygen consumption in the bradycardic phase of staphylococcal toxemia. The oxygen consumption was determined at room temperature (18-21°) in a resting state, before injection of staphylococcal toxin and 20-30 min thereafter, when the bradycardic phase had developed. By this time the heart rate had slowed to 70-100/min and the body temperature fallen by 0.5-1°.

The results given in the table show that the oxygen consumption in the bradycardic phase of staphylococcal toxemia fell on the average by 24.9%. The decrease in the oxygen expenditure in the initial bradycardic phase of staphylococcal toxemia, and the demonstration of its cholinergic nature [4, 9] confirm that the interpretation of this phase as anabolic is in fact correct.

The reaction of the adult dogs and puppies over the age of 2-2½ months to injection of staphylococcal toxin may be characterized as a whole by the statement that the organism, before responding with a stress reaction in the generally accepted meaning of the term, i.e., with tachycardia, tachypnea, a rise of body temperature, and an increase in basal metabolism, responds in the anabolic phase by a lowering of metabolism and of the level of activity of the respiratory and cardiovascular systems. Under these conditions the reserve powers for maintaining homeostasis in the subsequent tachycardiac (catabolic) phase are increased.

Previous investigations in the laboratory showed that the phased changes in the cardiac rhythm in young puppies (between 1 and 16-18 days old) after administration of dysentery, diphtheria, and typhoid toxins differed from those in adult animals, because of absence in the former of the constant tone of the vagus center, so that the cardiac activity is regulated by changes in the tone of the sympathetic innervation. Initially, when the latter is raised, a tachycardiac phase develops and later, when the tonic excitation of this center is lowered, the change to protracted collapse is observed, with a gradual slowing of respiration and of the heart rate and a lowering of the body temperature. In staphylococcal toxemia basically the same type of reaction is recorded, but consisting of only 2 phases. The anabolic phase is absent.

After injection of a lethal dose (0.5 ml/kg) of staphylococcal toxin into young puppies, the first, tachycardiac phase lasted 2-3 h. The range of the changes was small because of the high initial rhythm. The second, collapse phase, varied in its course. In some cases a slowly developing collapse, typical of this age, was observed (lasting 16-18 h), followed by death of the puppy (see Fig. 1V). In most experiments the collapse state developed more rapidly (in ½ -1 h, see Fig. 1 IV). Comparison of the phases of staphylococcal toxemia in adult dogs and in young puppies, as shown in Fig. 1, shows that whatever the character of the course of the collapse in the puppies, the state of homeostasis (the tachycardiac phase) lasted for a much shorter time in them than in the adult animals. In most cases death of the young puppies also occurred sooner than death of the adult dogs after injection of the same dose

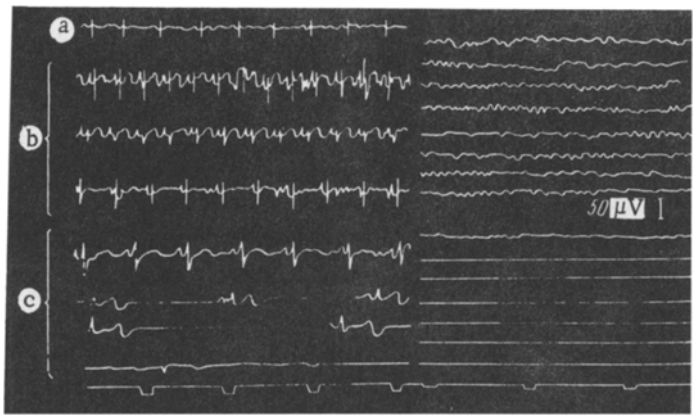

Fig. 3. ECG (left) and EEG (right) of a 6-day old puppy. A) Initial background; B) tachycardiac phase after injection of staphylococcal toxin in a dose of 0.5 ml/kg; C) phase of collapse. Time in seconds.

of staphylococcal toxin. Taking into consideration the criterion laid down in this laboratory for comparing the resistance of animals of different ages to stressors, namely by the duration of maintenance of homeostasis, it may be concluded that the dogs and older puppies in all cases were more resistant to staphylococcal toxin than young puppies, for, in the former, a state of homeostasis was maintained almost throughout the period of toxemia (with a dose of 0.5 ml/kg – 16-18 h), and only ceased a few minutes before death with the onset of prolonged or transient collapse.

The ECG and EEG of a 6-day old puppy at different periods after intravenous injection of a lethal dose of staphylococcal toxin are shown in Fig. 3. Tachycardia was maintained for 2 h, after which the heart rate gradually fell to 140-30/min, when the animal died. In the tachycardiac phase no significant changes were observed in the EEG. Both in the original EEG and in that taken during the tachycardiac phase a rhythm of 10-12/sec, of comparatively low amplitude, typical of puppies of this age was predominant. During the change to a state of collapse, the amplitude of the potentials began to fall, and the electrical activity subsequently disappeared, long before the cardiac activity ceased. The lower resistance of young puppies was attributed to the absence of an anabolic phase of the reaction in these animals, as demonstrated both by the indices of the ECG and by the character of the EEG.

In the puppies of an intermediate age – between 18 and 40 days – in most cases the first, bradycardic phase after injection of lethal doses of the toxin (0.5-1 ml/kg) was absent, despite the appearance at this age of the first signs of tonic excitation of the vagus center of cardiac innervation. In only 1 of 8 animals was a bradycardic phase observed, and it lasted 1 h 10 min. The absence of the initial bradycardia in the puppies of intermediate age may be attributed to the low resistance of the vagus center, which had only just started to function and which passed very swiftly into a state of inhibition.

Hence, although the initial reaction in young puppies and in those of intermediate age was outwardly similar, its mechanism was different. The distinguishing feature of the reactions of the puppies of intermediate age was that the course of collapse in these animals resembled that of collapse in the adults and not in the young puppies. A transient cardiac arrest developed, followed by a change to atrioventricular rhythm. Immediately after this first stage of collapse, vagal in origin, an automatic rhythm developed or the change took place to fibrillation.

SUMMARY

In adult dogs and in puppies over 2-2.5 months old fatal staphylococcus intoxication goes through 4 phases: bradycardic, tachycardiac and 2 collapse phases (syncope with vagus-escape, automatic rhythm of fibrillation). The first two phases are of importance homeostatic, especially the first bradycardiac, characterized by the anabolic orientation of metabolism and thus determining the whole course of the intoxication.

Only two phases are noted in young puppies (under 15 days of age); tachycardiac, of homeostatic significance, and collapse, when homeostasis is disturbed.

In puppies, aged from 18 to 40 days, intoxication followed 3 phases: a tachycardiac and 2 collapse phases, pursuing the same course as in adults.

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